

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

Date of mailing (day/month/year) 25 May 1998 (25.05.98)	From the INTERNATIONAL BUREAU To:  United States Patent and Trademark Office (Box PCT) Crystal Plaza 2 Washington, DC 20231 ETATS-UNIS D'AMERIQUE  in its capacity as elected Office
International application No. PCT/US97/18514	Applicant's or agent's file reference 5500-01-TMC
International filing date (day/month/year) 09 October 1997 (09.10.97)	Priority date (day/month/year) 11 October 1996 (11.10.96)
Applicant ALBRECHT, Hans, P. et al.	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:  
30 April 1998 (30.04.98)

in a notice effecting later election filed with the International Bureau on:  
\_\_\_\_\_

2. The election  was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35 Form PCT/IB/331 (July 1992)	Authorized officer A. Addae-Ruesch  Telephone No.: (41-22) 338.83.38
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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 97/18514

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07C271/22 C07C233/47 C07C233/51 C07C311/19 C07D333/24

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 6 C07C C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 618 223 A (SANDOZ) 5 October 1994 see claims 1,10; example 31 ----	1,30
X	ADNAN M.M. MJALLI ET AL : "Inhibition of interleukin-1beta converting enzyme by N-acyl-aspartic acid ketones" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 5, no. 13, 1995, pages 1405-1408, XP002053982 see page 1405; examples 3J-N ----	1,30
X	ADNAN M.M. MJALLI ET AL: "Activated ketones as potent reversible inhibitors of interleukin-1beta converting enzyme" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 4, no. 16, 1994, pages 1965-1968, XP002054017 see page 1965; example 4C ----	1,30
		-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

### \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

4

Date of the actual completion of the international search

30 January 1998

Date of mailing of the international search report

19. 02. 98

Name and mailing address of the ISA

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Authorized officer

Voyiazoglou, D

**INTERNAL SEARCH REPORT**Internal Application No  
PCT/US 97/18514**C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 623 592 A (STERLING) 9 November 1994 see claims 1,3 -----	1,30,43

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 97/18514

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: 21-29  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claim(s) 21-29  
is(are) directed to a method of treatment of the human/animal  
body, the search has been carried out and based on the alleged  
effects of the compound/composition.
2.  Claims Nos.: 1-18, 20, 30  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such  
an extent that no meaningful International Search can be carried out, specifically:  
The claims are so broad that to determining the scope of a meaningful  
search due account has been taken of Rule 33.3 PCT, special emphasis was  
put on the subject matter of claims 19, 31-40, 43
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all  
searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment  
of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report  
covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is  
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

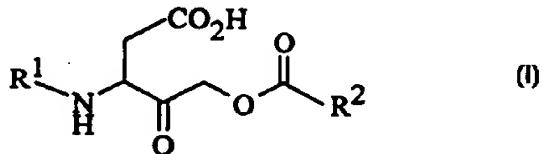
PCT/US 97/18514

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP 618223 A	05-10-94	CA 2117121 A		09-09-94
		JP 6340691 A		13-12-94
EP 623592 A	09-11-94	AU 676887 B		27-03-97
		AU 6075294 A		03-11-94
		CA 2122227 A		30-10-94
		CZ 9401035 A		16-11-94
		FI 942005 A		30-10-94
		HU 68563 A		28-06-95
		JP 7025865 A		27-01-95
		NO 941580 A		31-10-94
		NZ 260410 A		25-06-96
		SK 50294 A		08-02-95



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C07C 271/22, 233/47, 233/51, 311/19, C07D 333/24		A1	(11) International Publication Number: <b>WO 98/16502</b> (43) International Publication Date: 23 April 1998 (23.04.98)
(21) International Application Number: PCT/US97/18514			(US). PARA, Kimberly, Suzanne [US/US]; 2735 Dexter Avenue, Ann Arbor, MI 48103 (US). THOMAS, Anthony, Jerome [US/US]; 2909 Brockman, Ann Arbor, MI 48104 (US). WALKER, Nigel [GB/DE]; Frauengasse 20, D-69221 Dossenheim (DE).
(22) International Filing Date: 9 October 1997 (09.10.97)			
(30) Priority Data: 60/028,322 11 October 1996 (11.10.96) US			(74) Agents: RYAN, M., Andrea; Warner-Lambert Company, 201 Tabor Road, Morris Plains, NJ 07950 (US) et al.
(71) Applicant (for all designated States except US): WARNER-LAMBERT COMPANY [US/US]; 201 Tabor Road, Morris Plains, NJ 07950 (US).			(81) Designated States: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).
(72) Inventors; and			
(75) Inventors/Applicants (for US only): ALBRECHT, Hans, P. [DE/DE]; Am Wetzelsberg 59, D-69517 Goxheimertal (DE). ALLEN, Hamish, John [GB/US]; 47 Eastern Point Drive, Shrewsbury, MA 01545 (US). BRADY, Kenneth, Dale [US/US]; 32 Ivernia Road, Worcester, MA 01606 (US). CAPRATHE, Bradley, William [US/US]; 31480 Myrna, Livonia, MI 48154 (US). GILMORE, John, Lodge [US/US]; Apartment 178C, 3695 Greenbrier Boulevard, Ann Arbor, MI 48105 (US). HARTER, William, Glen [US/US]; 3750 Shagbark, Chelsea, MI 48118 (US). HAYS, Sheryl, Jeanne [US/US]; 2729 Aspen Road, Ann Arbor, MI 48108 (US). KOSTLAN, Catherine, Rose [US/US]; 9876 Moon Road, Saline, MI 48176 (US). LUNNEY, Elizabeth, Ann [US/US]; 619 Ridgewood Court, Ann Arbor, MI 48103			

(54) Title: ASPARTATE ESTER INHIBITORS OF INTERLEUKIN-1 $\beta$  CONVERTING ENZYME

## (57) Abstract

The present invention relates to compounds that are inhibitors of interleukin-1 $\beta$  converting enzyme that have formula (I). This invention also relates to a method of treatment of stroke, inflammatory diseases, reperfusion injury, Alzheimer's disease, and shigellosis, and to a pharmaceutically acceptable composition that contains a compound that is an inhibitor of interleukin-1 $\beta$  converting enzyme.

**PATENT COOPERATION TREATY**  
**PCT**

**INTERNATIONAL SEARCH REPORT**

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>5500-01-TMC</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 97/ 18514</b>	International filing date (day/month/year) <b>09/10/1997</b>	(Earliest) Priority Date (day/month/year) <b>11/10/1996</b>
Applicant <b>WARNER-LAMBERT COMPANY et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1.  Certain claims were found unsearchable (see Box I).
2.  Unity of invention is lacking (see Box II).
3.  The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing
  - filed with the international application.
  - furnished by the applicant separately from the international application,
    - but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
  - Transcribed by this Authority
4. With regard to the title,  the text is approved as submitted by the applicant.
  - the text has been established by this Authority to read as follows:
5. With regard to the abstract,
  - the text is approved as submitted by the applicant.
  - the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.
6. The figure of the **drawings** to be published with the abstract is:
  - Figure No. ---  as suggested by the applicant.
  - because the applicant failed to suggest a figure.
  - because this figure better characterizes the invention.
  - None of the figures.

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US 97/18514

**Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)**

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**Remark:** Although claim(s) 21-29  
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**The claims are so broad that to determining the scope of a meaningful  
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**Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)**

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restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 97/18514

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Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07C C07D

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	-/-	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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"O" document referring to an oral disclosure, use, exhibition or other means

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&amp;" document member of the same patent family

4

Date of the actual completion of the international search

Date of mailing of the international search report

30 January 1998

19.02.98

## Name and mailing address of the ISA

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NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

## Authorized officer

Voyiazoglou, D

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 97/18514

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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		JP 6340691 A		13-12-94
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		JP 7025865 A		27-01-95
		NO 941580 A		31-10-94
		NZ 260410 A		25-06-96
		SK 50294 A		08-02-95